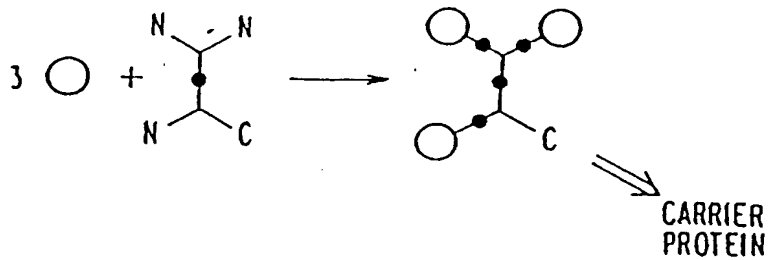
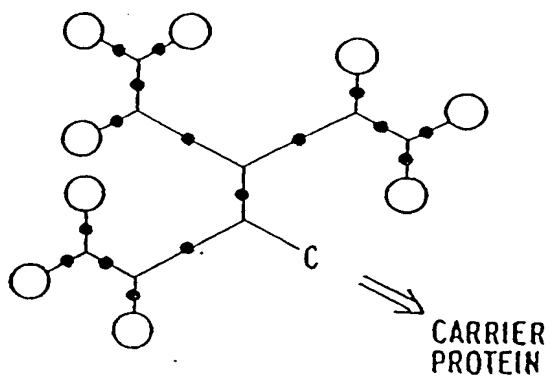
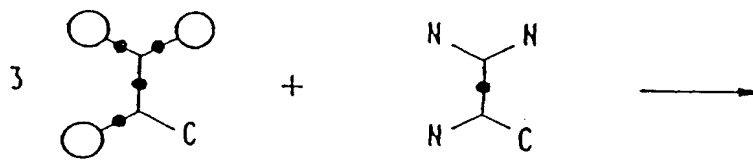


TRIVALENT
CONJUGATE



NONVALENT
CONJUGATE



○ T_n -ANTIGEN

- AMIDE BOND

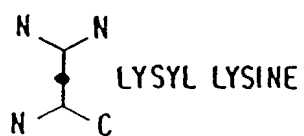


FIG. 1 A

SCHEME II

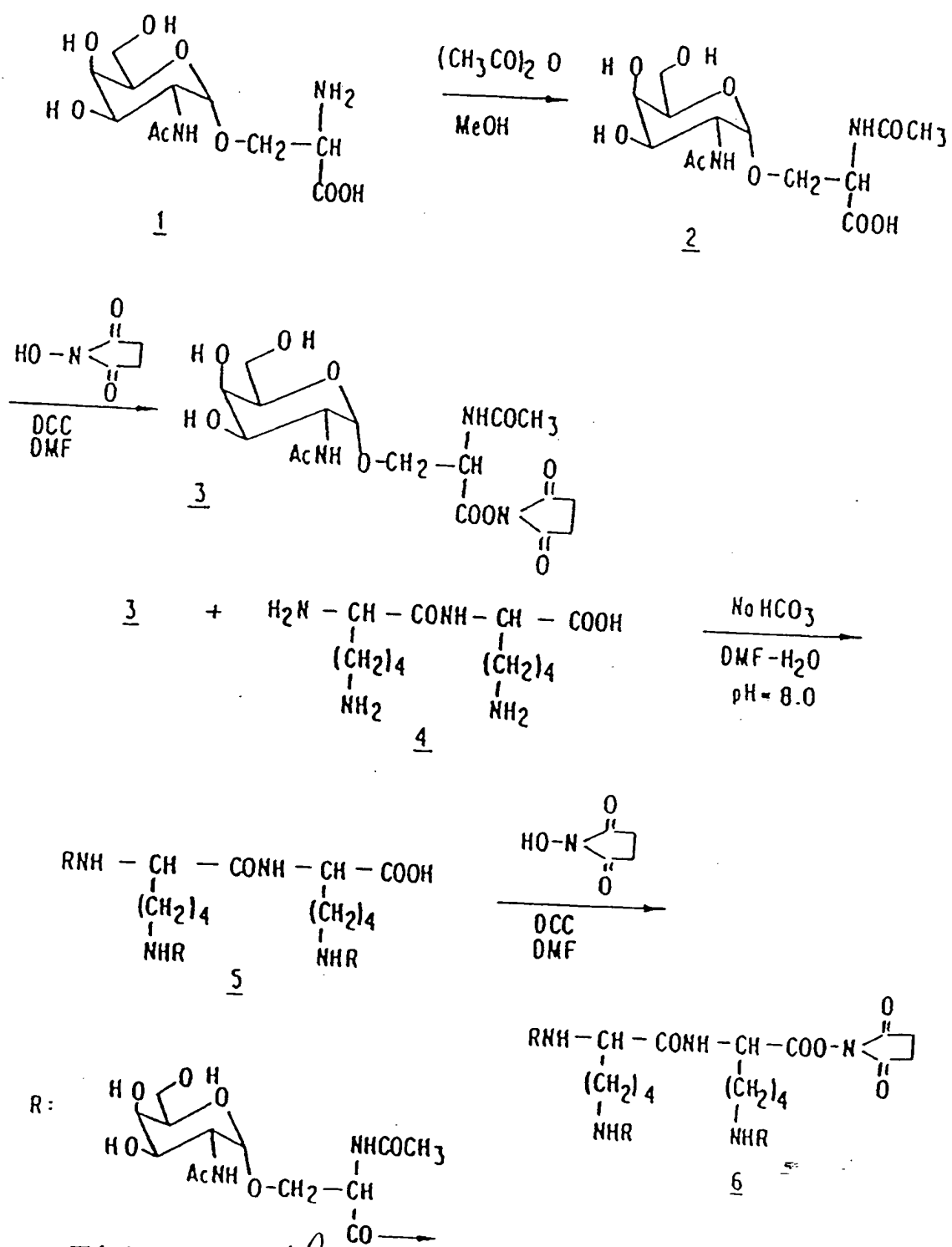


FIG.

1β

SYNTHESIS OF ANTIGEN CLUSTERS.

General formula: $\text{Ac}-(\text{Ser})_m-(\text{Thr})_n-\text{NH}-(\text{CH}_2)_3-\text{COOH}$
 $(m + n \leq 3)$

Examples: $\text{Ac}-\underset{*}{\text{Ser}}-\text{NH}-(\text{CH}_2)_3-\text{COOH}$ 5

$\text{Ac}-\underset{*}{\text{Thr}}-\text{NH}-(\text{CH}_2)_3-\text{COOH}$

$\text{Ac}-\underset{*}{\text{Ser}}-\underset{*}{\text{Ser}}-\text{NH}-(\text{CH}_2)_3-\text{COOH}$

$\text{Ac}-\underset{*}{\text{Ser}}-\underset{*}{\text{Ser}}-\underset{*}{\text{Ser}}-\text{NH}-(\text{CH}_2)_3-\text{COOH}$

$\text{Ac}-\underset{*}{\text{Ser}}-\underset{*}{\text{Thr}}-\underset{*}{\text{Thr}}-\text{NH}-(\text{CH}_2)_3-\text{COOH}$ 6

* : $\text{GalNAc}\alpha 1 \longrightarrow / \text{NeuAc}\alpha 2 \longrightarrow 6\text{GalNAc}\alpha 1 \longrightarrow$

FIG.

2A

CONSTRUCTION OF MULTIVALENT SYSTEMS.

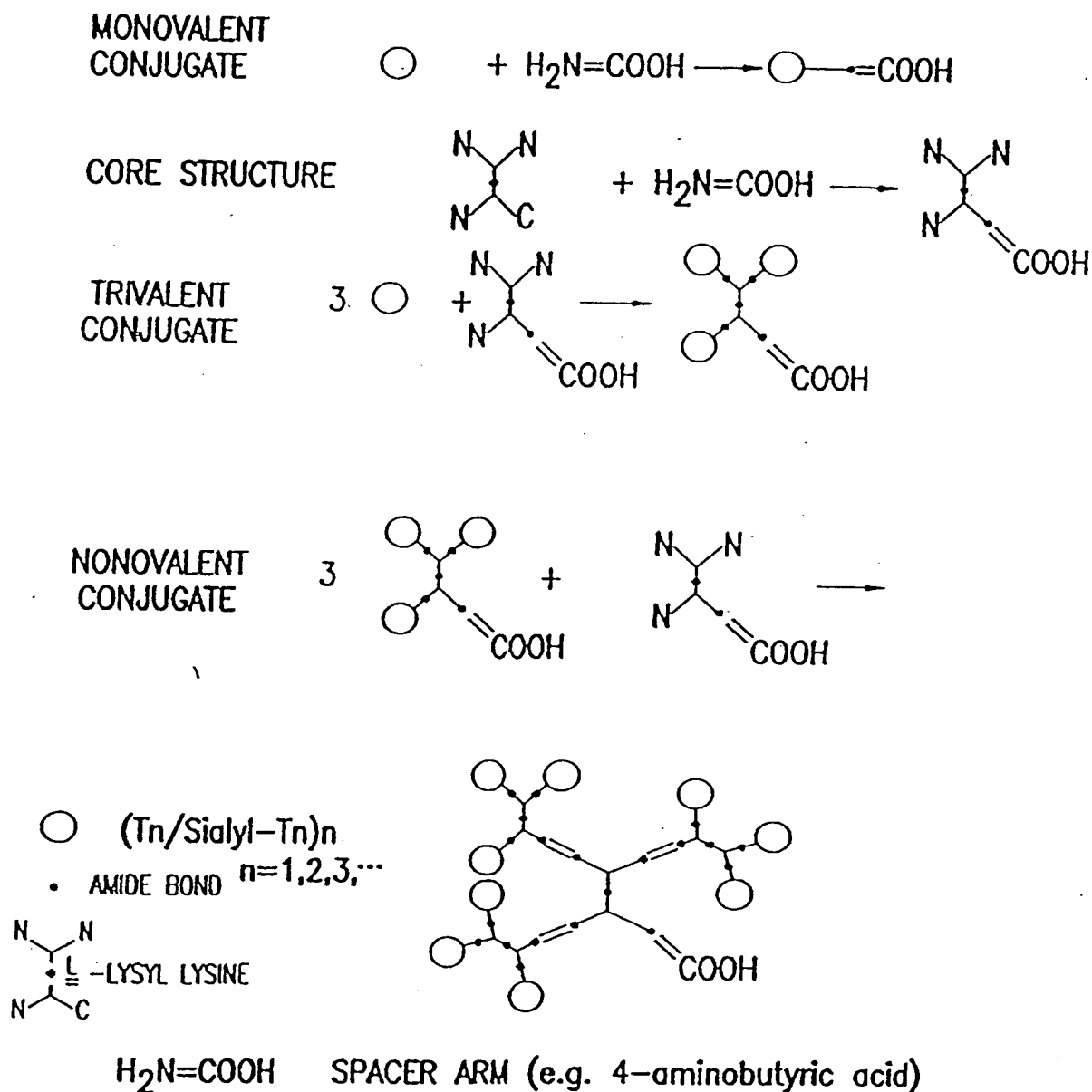


FIG.

213

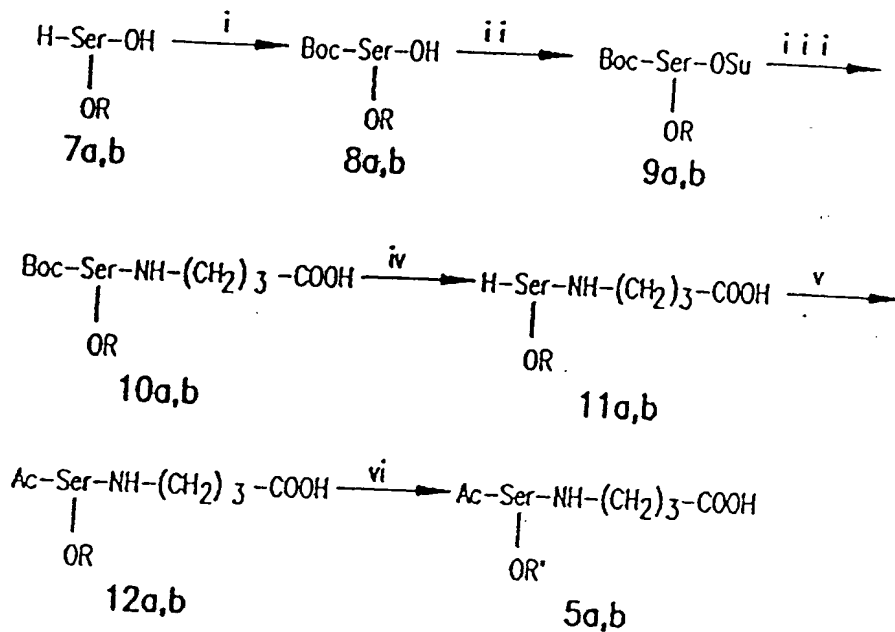
DESIGN FOR EFFECTIVE PRESENTATION OF SYNTHETIC ANTIGENS TO IMMUNE SYSTEM.

- (☐)_h — carrier protein (e.g. BSA, KLH)
- ☐ — tripalmitoyl-S-glycerylcysteinyl-seryl-serine
- ☐ — monophosphoryl lipid A
- ☐ : constructed antigen systems

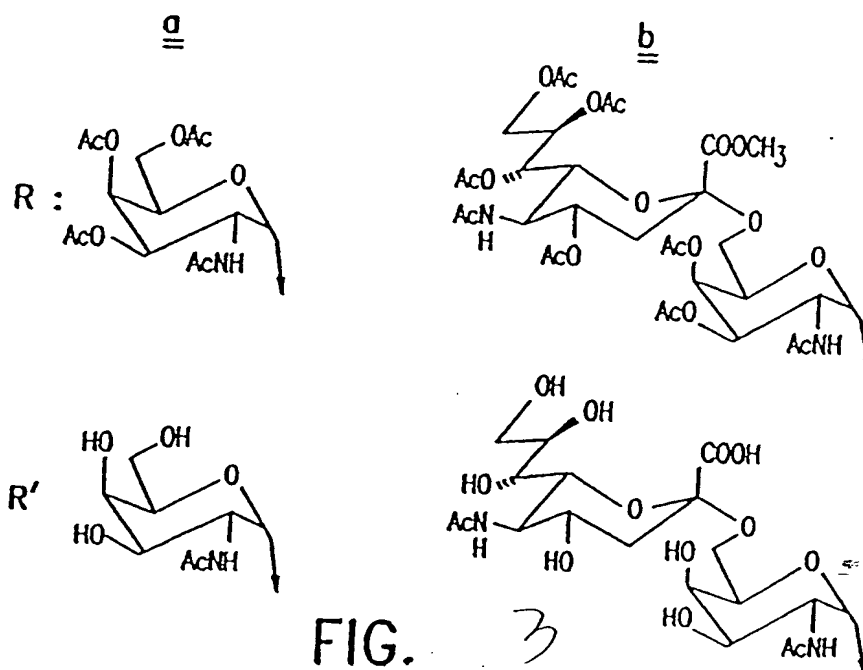
FIG.

26

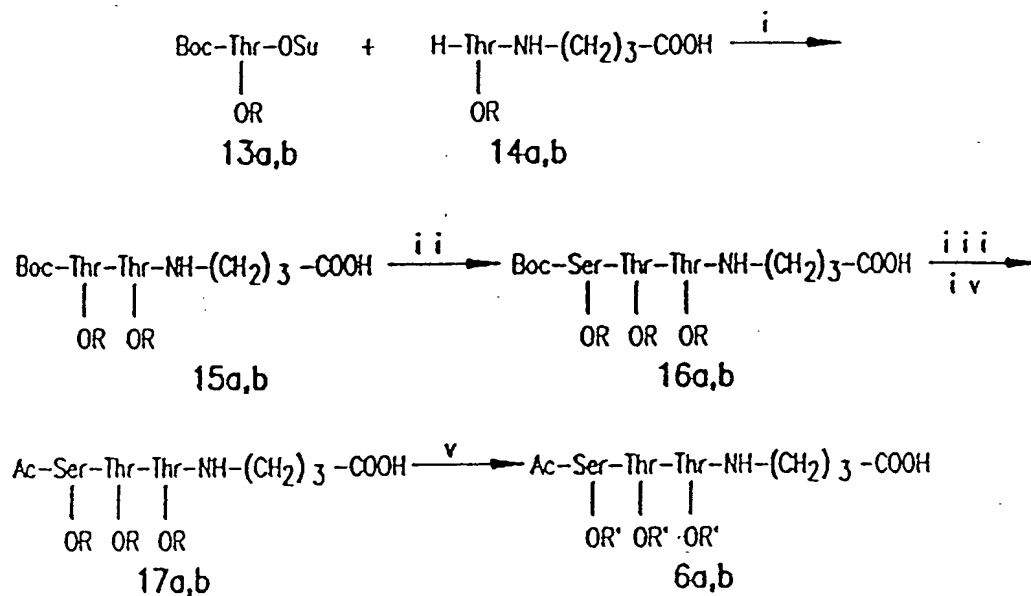
SYNTHESIS OF 5



Reagents: i) Boc_2O , Et_3N , MeOH ; i i) NHS , EDC , CH_2Cl_2 ;
i i i) $\text{H}_2\text{N-(CH}_2\text{)}_3\text{-COOH}$, Et_3N , DMF ; iv) HCOOH ; v) Ac_2O , MeOH ;
vi) 10% 1N NaOH in MeOH , 5 min.



SYNTHESIS OF 6



Reagents: i) Et₃N, DMF; ii) 9a,b, Et₃N, DMF; iii) HCOOH;
iv) Ac₂O, MeOH; v) 10% 1N NaOH in MeOH, 1 h.

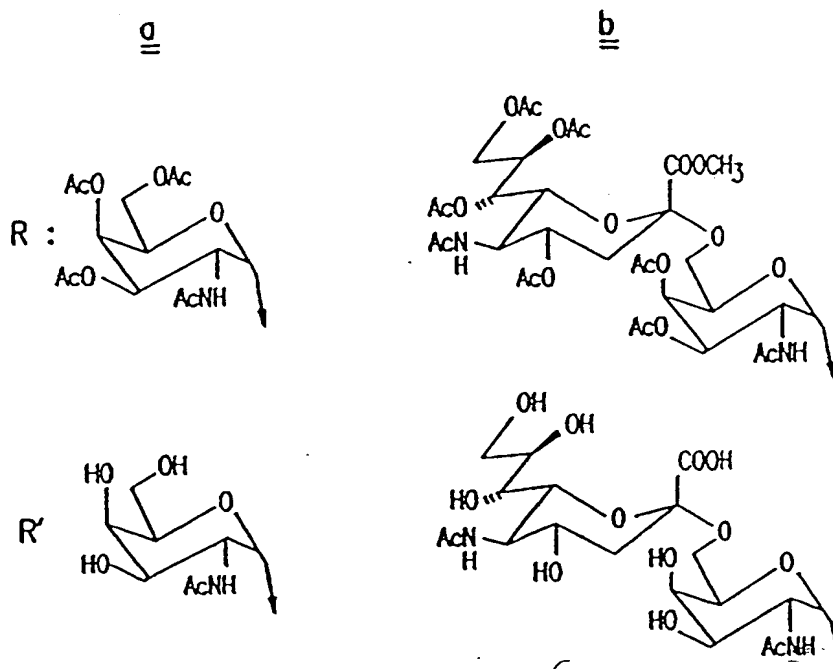
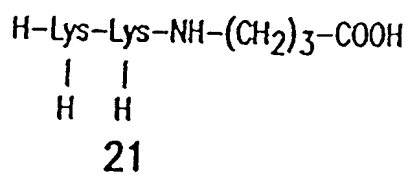
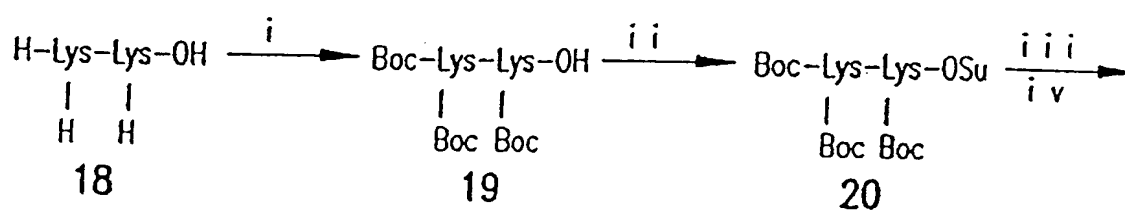


FIG. 4

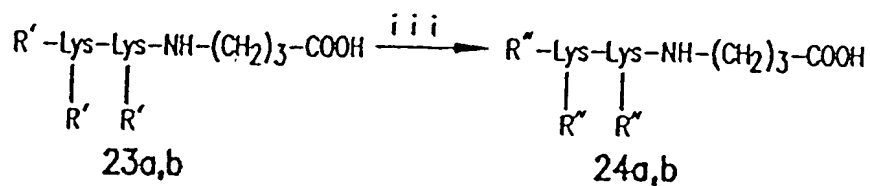
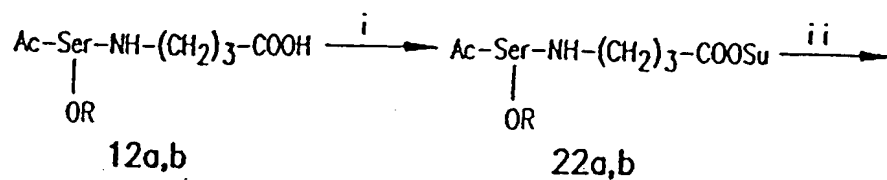
PREPARATION OF CORE STRUCTURE



Reagents: i) Boc_2O , Et_3N , MeOH ; i i) NHS , EDC , CH_2Cl_2 ;
i i i) $\text{H}_2\text{N-(CH}_2\text{)}_3\text{-COOH}$, Et_3N , DMF ; iv) HCOOH .

FIG. 1

5X



Reagents: i) NHS, EDC, DMF; i i) 21, Et₃N, DMF-H₂O;
i i i) 10% 1N NaOH in MeOH, 5 min.

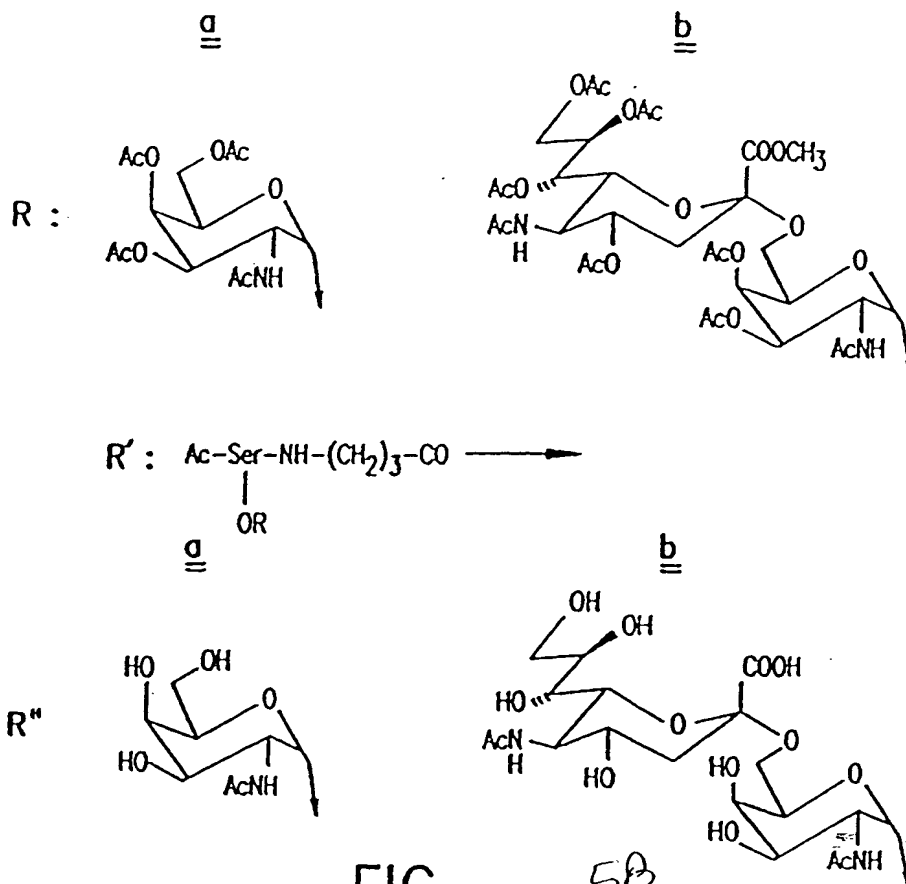
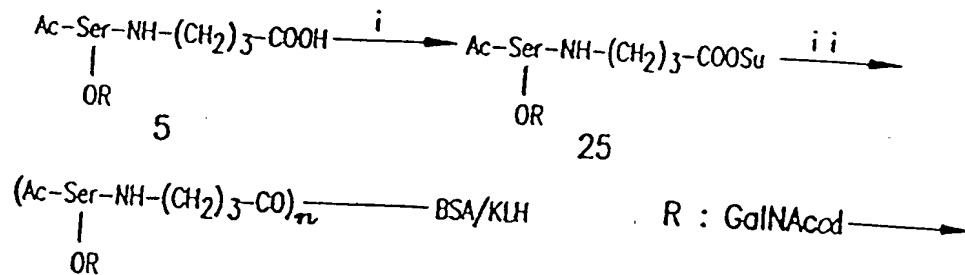


FIG.

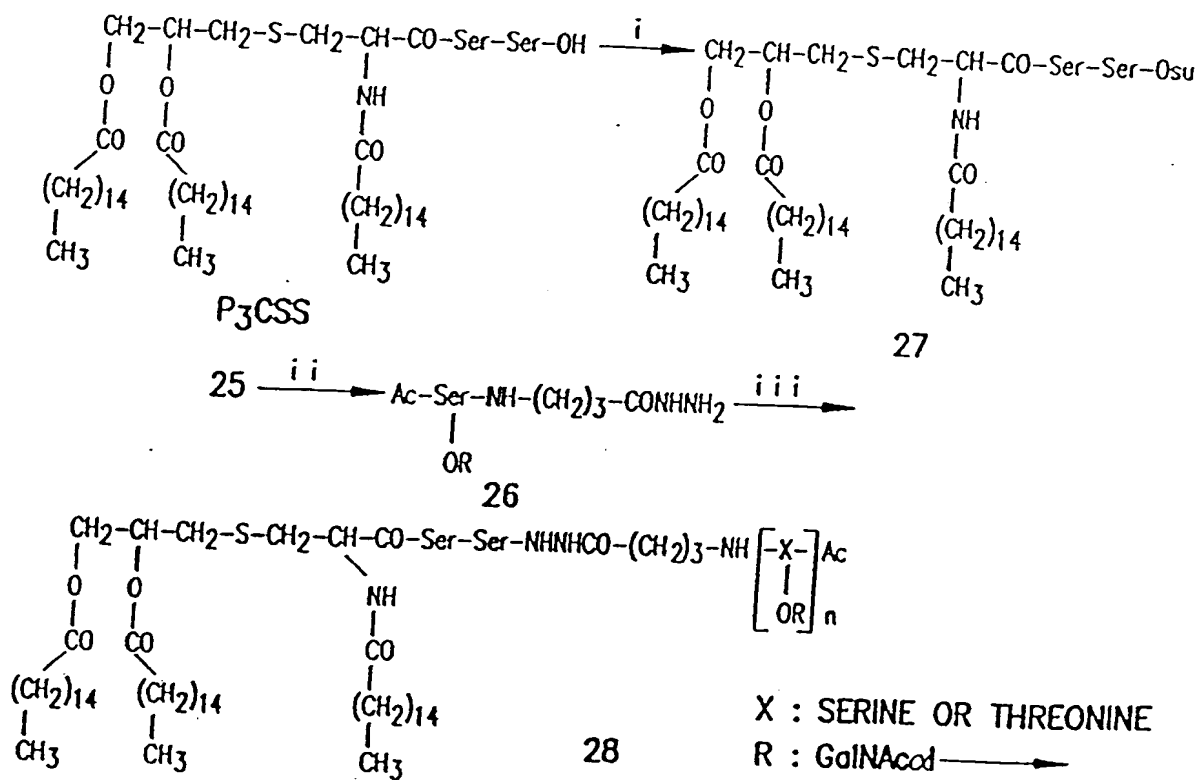
5B

CONJUGATION WITH CARRIER PROTEINS



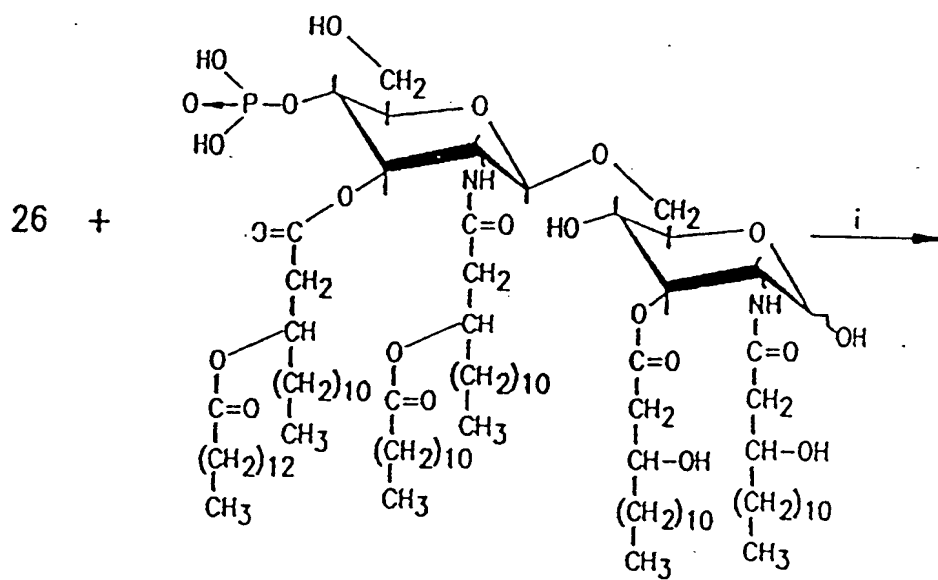
Reagents: i) NHS, EDC, DMF; i i) BSA/KLH, NaHCO_3 , DMF- H_2O .

CONJUGATION WITH NON-MACROMOLECULES

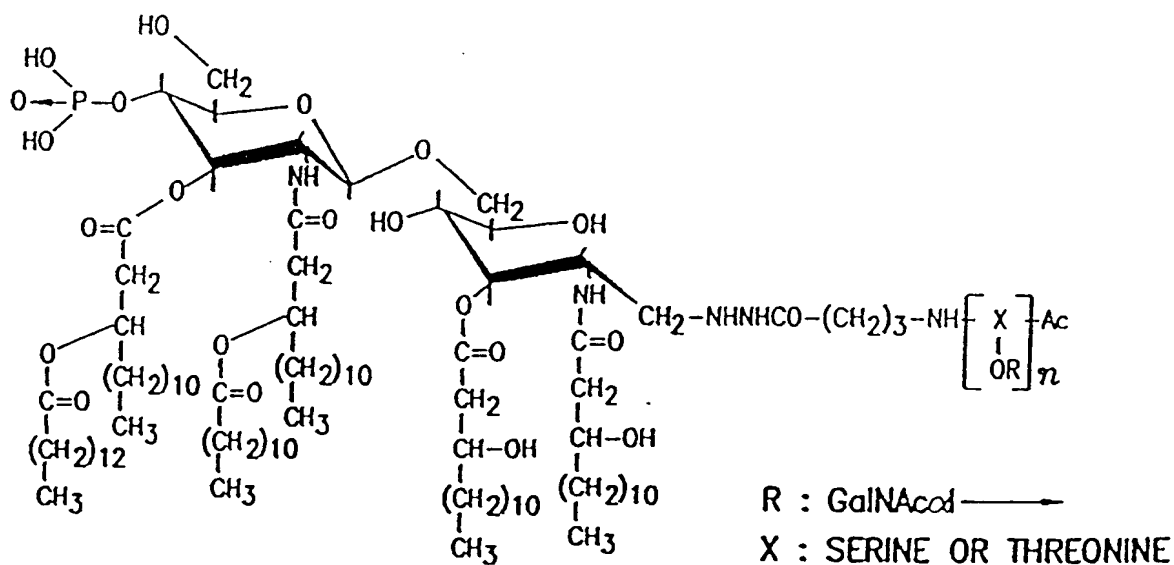


Reagents: i) NHS, EDC, CH_2Cl_2 ; ii) NH_2NH_2 , aq MeOH ; iii) $\text{DMF-H}_2\text{O}$.

FIG. 6A



MPL

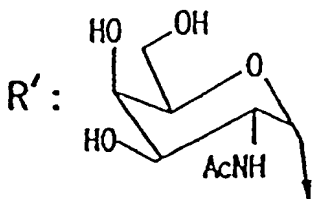
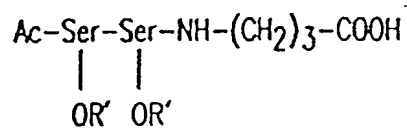
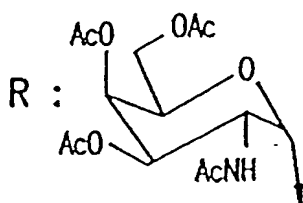
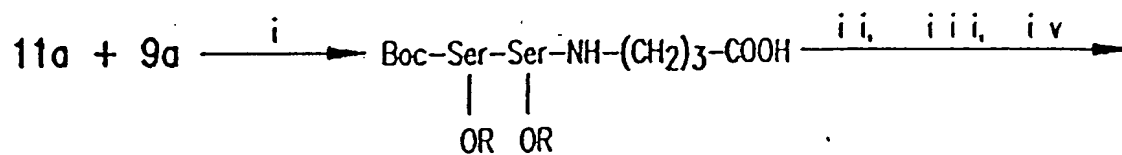


29

Reagents: i) NaCNBH₃, NaHCO₃, H₂O.

FIG.

6B



Reagents: i) Et₃N, DMF; ii) HCOOH; iii) Ac₂O, MeOH; iv) 10% 1N NaOH-MeOH, 5 min.

FIG. 8

Fig.9 A

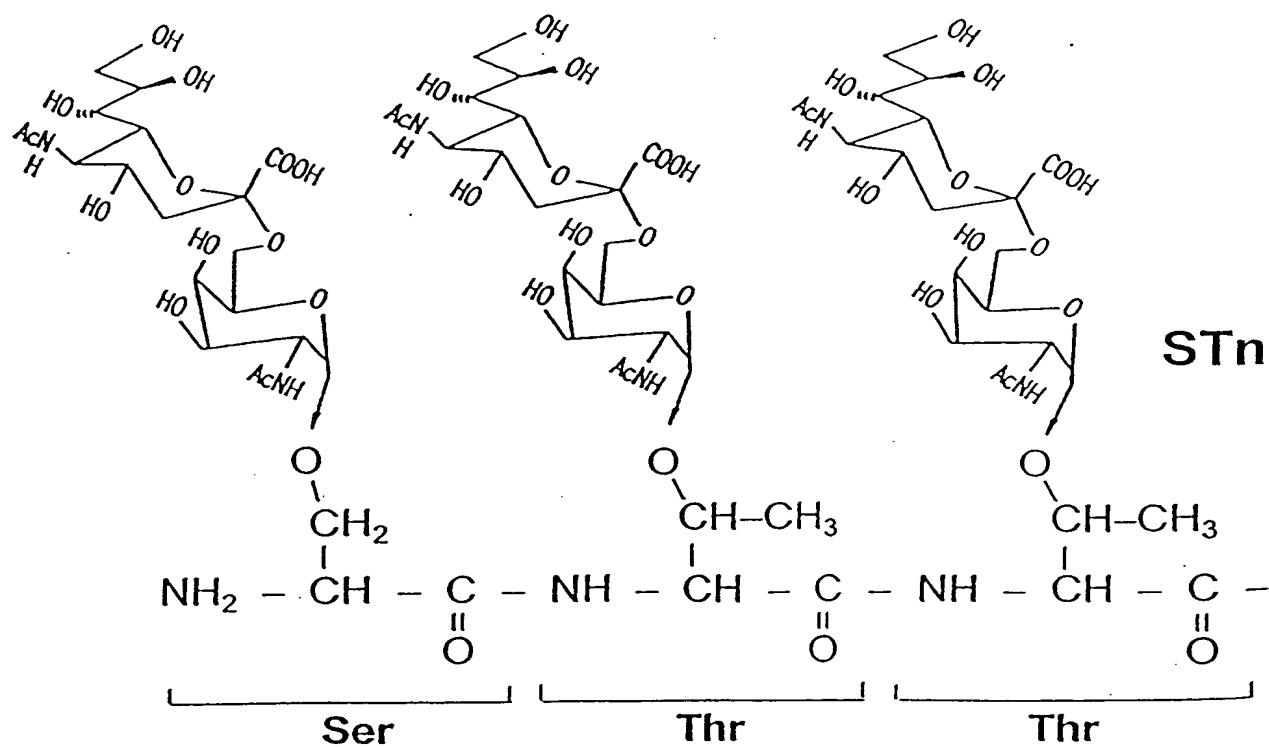
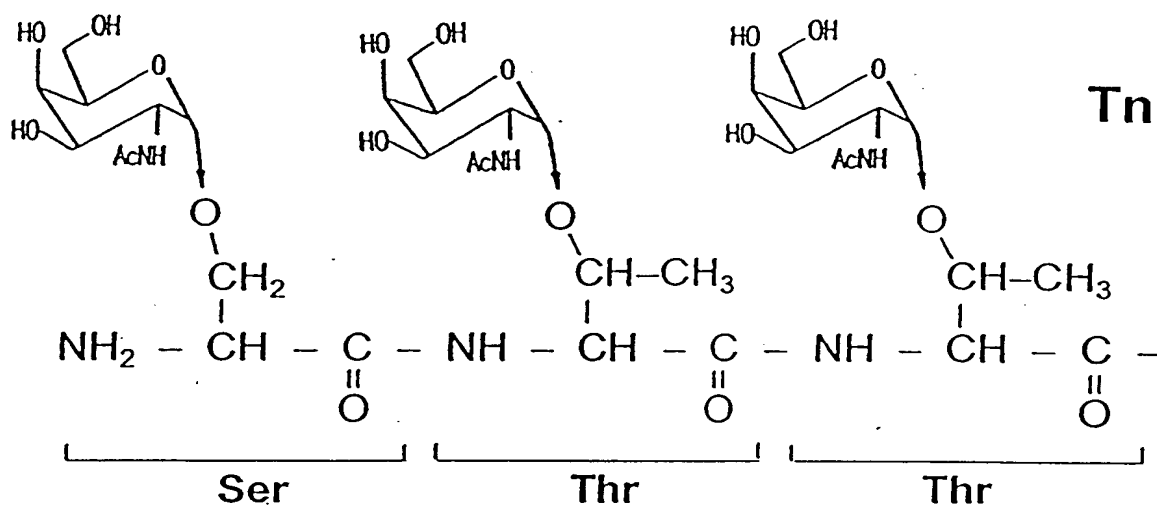
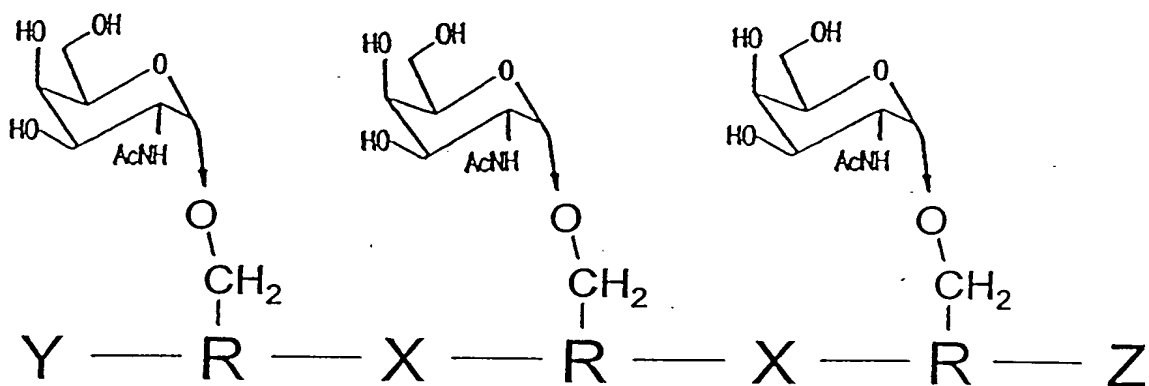


Fig. 9B



Y = terminal protected residue. X = spacer.

Z = active functional group ready to link to core or carrier molecule (e.g. activated carboxyl)

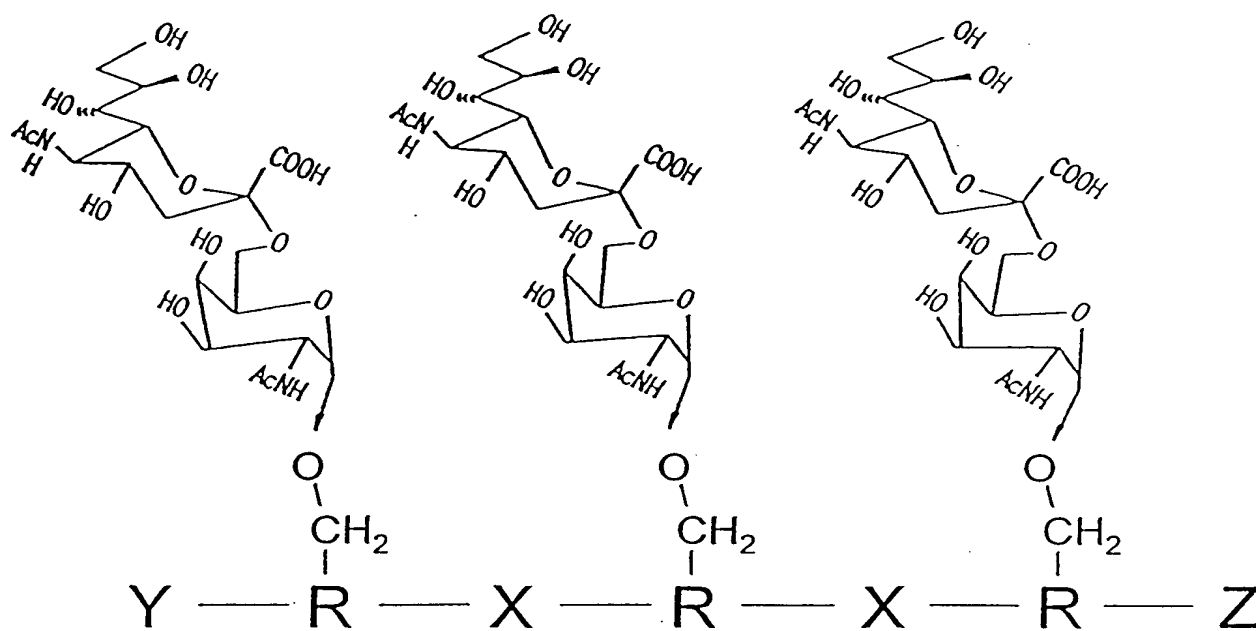


Figure 10

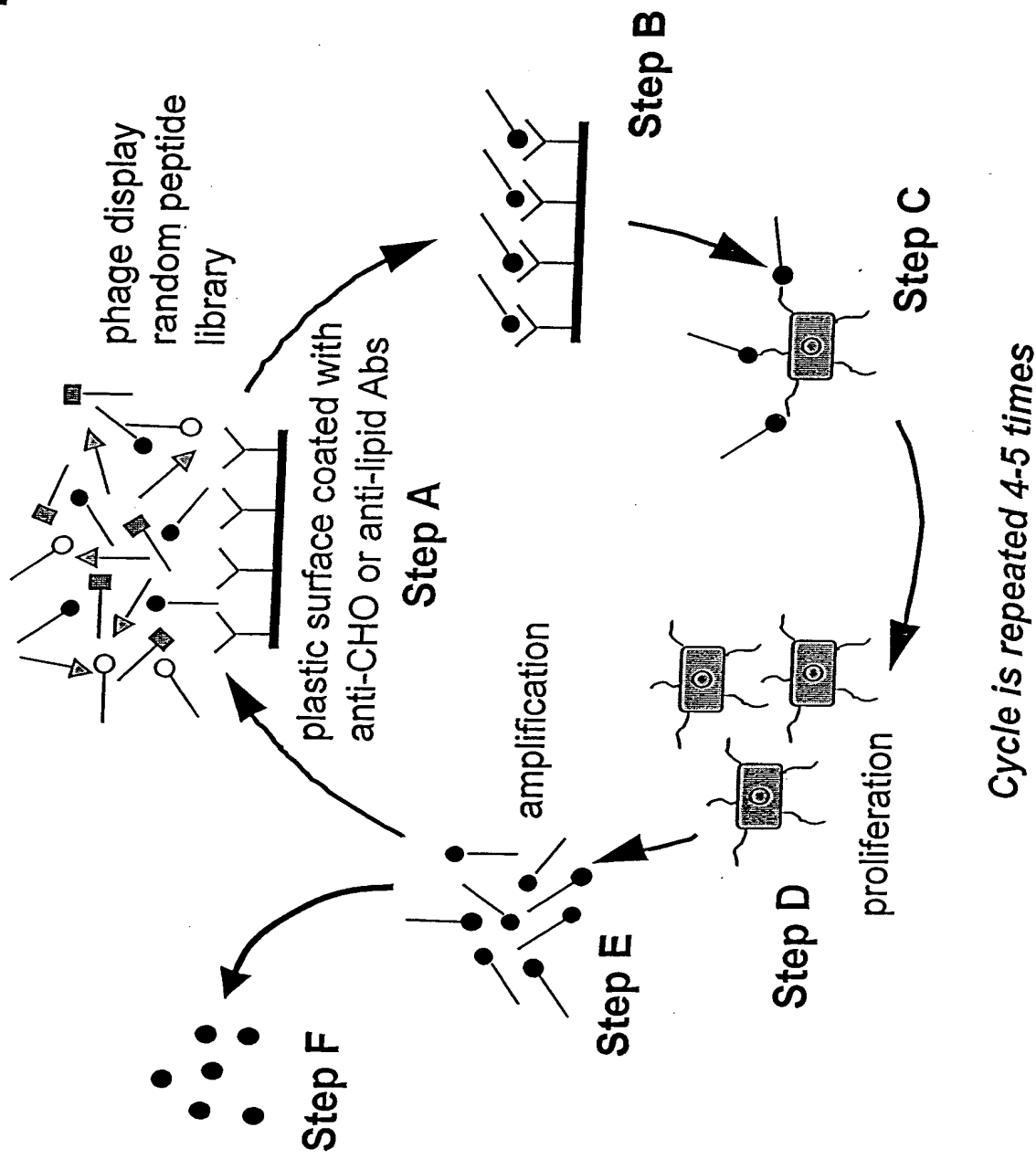


Figure 11A. Class II MHC restricted presentation of extracellular antigen to CD4+ T helper cells.

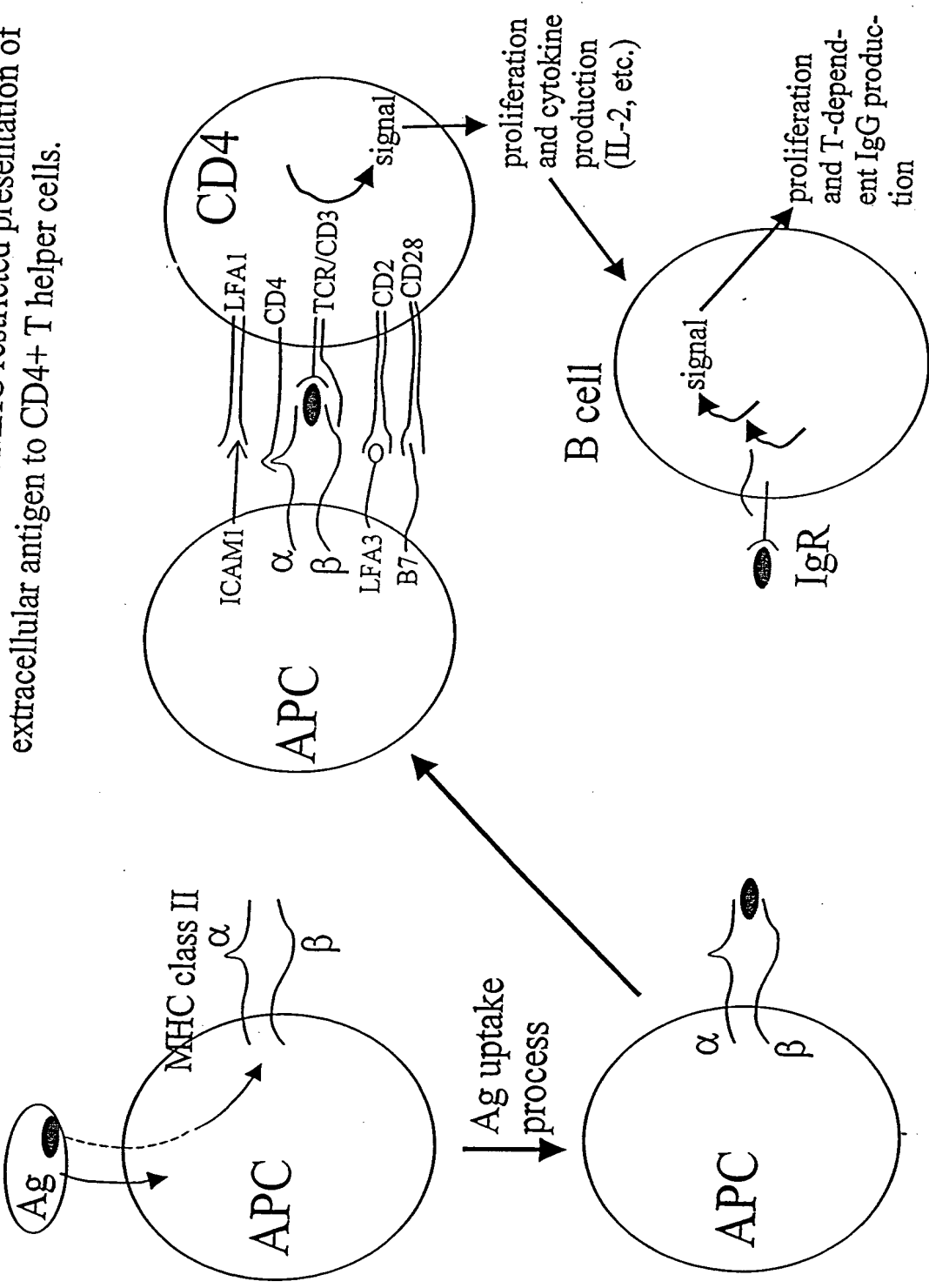


Fig. 12

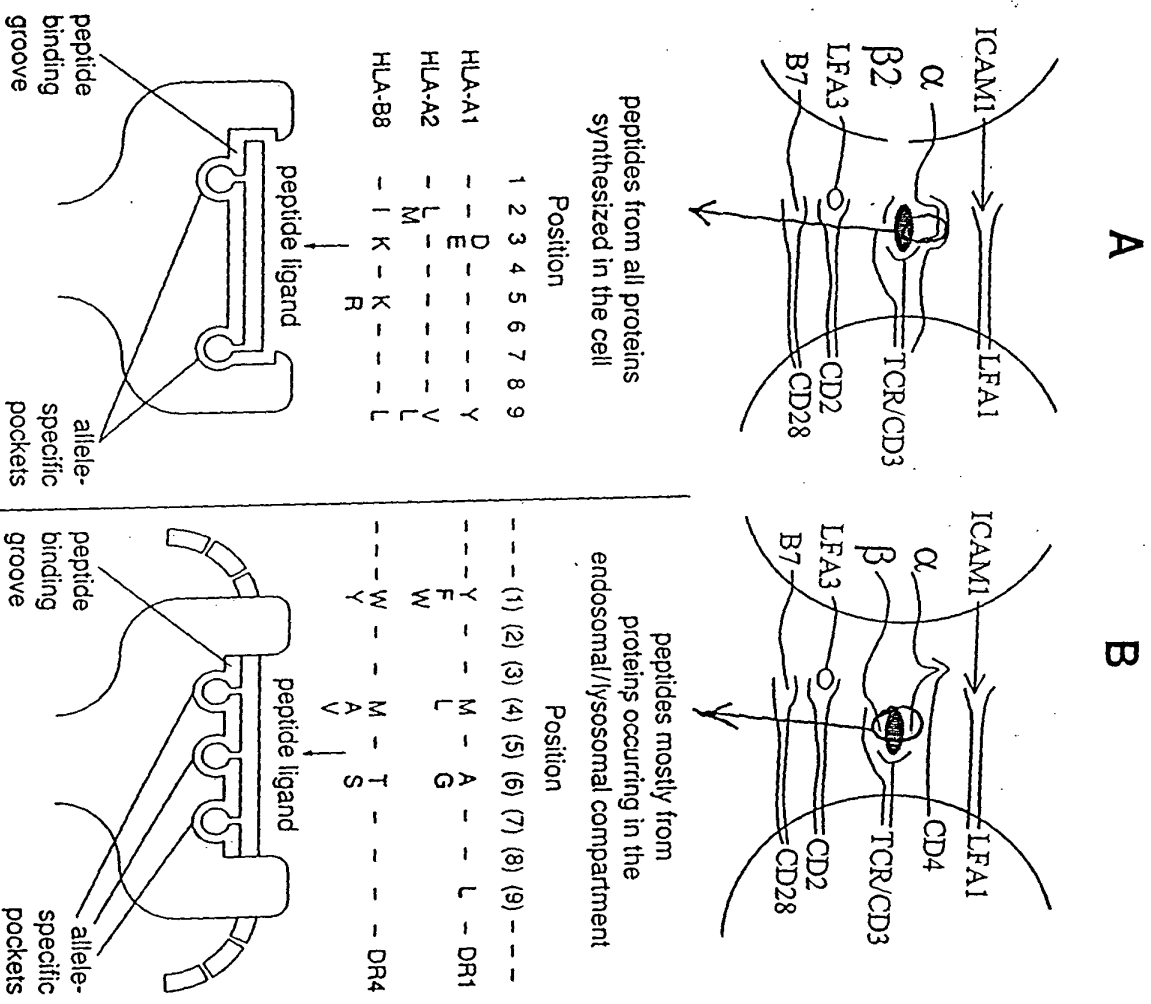


Figure 13

